Atrial fibrillation patient preferences for oral anticoagulation and stroke knowledge:

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Atrial fibrillation patient preferences for oral anticoagulation and stroke knowledge: results of a conjoint analysis

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Conflicts of interests

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SUMMARY

Background*:* Guidelines recommend that patients with atrial fibrillation (AF) are involved in oral anticoagulant (OAC) treatment decisions. Understanding which OAC attributes AF patients value most could help optimize treatment.

Methods*:* A cross-sectional online survey was conducted in patients with nonvalvular AF taking an OAC for stroke prevention in the United States, Canada, Germany, France, and Japan. Patients were asked about their stroke knowledge, perception of the seriousness of AF and concern about stroke, and to rank seven OAC attributes in order of importance. A conjoint analysis was performed to determine the inherent value of four attributes.

Results*:* 937 patients (mean [SD] 54.3 [16.6] years; 37.1% female) participated. Of these, 19.5%, 27.9%, and 29.8% had good, moderate, and low stroke knowledge, respectively; 22.8% had no stroke knowledge. Overall, 39.4% of patients (47.5% with good stroke knowledge) perceived AF as very/extremely serious.

The OAC attribute ranked as most important was stroke prevention followed by major bleeding risk, other side effects, dosing frequency, antidote availability, dietary restrictions and use with/without food. In the conjoint analysis, stroke risk reduction was the most valued property, followed by reduction in major bleeding risk, less frequent administration, and administration with/without food. Preferences did not differ with level of stroke knowledge, perception of seriousness of AF, concern of stroke, or medication burden.

Conclusions*:* Most AF patients consider efficacy and safety to be the most important OAC attributes, whereas dosing frequency was deemed as less important.

KEYWORDS

atrial fibrillation, conjoint analysis, oral anticoagulants, stroke knowledge, patient preference

1 INTRODUCTION

Current treatment guidelines for stroke prevention in patients with atrial fibrillation (AF) recommend patient involvement in decisions, [1-3] to improve adherence to medication and clinical outcomes. [1,4] However, many AF patients have a poor understanding of the condition and limited knowledge regarding stroke and oral anticoagulants (OACs). [4-9] Many studies of stroke knowledge have been conducted in the general population [10-15] and in individuals with a variety of stroke risk factors [16] rather than AF patients specifically, and to our knowledge, the relationship between stroke knowledge and OAC preferences in the AF population has not been assessed.

A better understanding of the patient viewpoint, and the extent to which patients value individual OAC attributes, could help physicians to decide on the most appropriate treatment in collaboration with the patient, as recommended by the guidelines.

The objective of our study was to assess the relationship between patients' stroke knowledge and their preferences for specific OAC attributes, using 2 methods: (i) a ranking exercise and (ii) a choice-based conjoint analysis. The study also assessed whether patient preferences differed with respect to medication burden, perception of seriousness of AF, concern about stroke, and whether patients had a recent or established AF diagnosis, with or without a recent stroke.

2 METHODS

A cross-sectional, multinational (the United States, Canada, Germany, France, and Japan) survey was conducted in adults (≥18 years) with nonvalvular AF receiving an OAC for stroke

prevention. Patients were recruited through consumer panels, or by telephone or face-to-face contact resulting from referrals from physicians, nurses or other patients, or from patient associations or social media. Patients were stratified into three groups: newly diagnosed AF (within the previous 6 months; [12 months in Japan]) without recent stroke; established AF (diagnosed between 7–24 months previously;[1–3 years previously in Japan]) without recent stroke; and AF (diagnosed at any time) with a recent stroke (within the past 6 months).

Patients completed a 30-minute online questionnaire on stroke knowledge, perception of AF and stroke, current medication burden, and views on OACs. Three open-ended questions on etiology, stroke symptoms, and risk factors were used to categorize patients as having a good, moderate, or low level of stroke knowledge, or no stroke knowledge, using a predefined scoring system (Supplemental Table 1).

Patients were asked how many different medications they took daily; the daily frequency of their oral medication; how serious they considered AF to be; how frequently they were concerned by stroke risk; how much they wanted to be involved in OAC treatment decisions; and which sources they used, if any, to obtain information regarding their current OAC.

Patients were asked how familiar they were with standardized information regarding AF, stroke, and the potential benefits and risks of OACs (Supplemental Table 2).

2.1 Ranking Exercise

Before being exposed to the standardized information, patients ranked by order of importance the following OAC attributes (which were presented in a random order): stroke prevention, major bleeding risk, other side effects, dosing frequency, antidote availability, dietary restrictions, and whether medication needed to be taken with food.

2.2 Choice-based Conjoint Analysis

After the standardized information had been presented, patients were asked which of three hypothetical products they would be most willing to take to prevent a stroke. Each product profile was characterized by specific levels for four attributes: stroke risk reduction, major bleeding risk, frequency of administration, and administration with/without food (Figure 1; Supplemental Table 3). For each hypothetical product, stroke risk was either the same as, or 21% or 36% lower than standard therapy; major bleeding risk was either the same as, or 20% or 31% lower than standard therapy. These figures were based on the results of ARISTOTLE and RE-LY, where the rate of stroke was 21% and 36% lower with apixaban and dabigatran (150 mg), respectively vs warfarin and the major bleeding rate was 31% and 20% lower with apixaban and dabigatran (110 mg), respectively vs warfarin. [17-19] Each hypothetical product was dosed once or twice daily and could be taken with or without food.

Patients were asked to perform the hypothetical product selection a total of ten times. The utility value of each characteristic was determined using logistic regressions based on a Bayesian analysis. Points were awarded to each attribute level every time it appeared in the patient's chosen hypothetical product profile (+1 if chosen, –1 if not chosen, 0 if not presented) and each attribute level was given a utility value.

Results were assessed for the overall study population and according to AF subgroups, stroke knowledge, medication burden, perceived seriousness of AF, and concern about stroke risk. Three quality control assessments, increasing in stringency, were included to ensure that patients gave considered answers rather than random responses (Supplementary Table 4).

Descriptive statistics are presented as mean and standard deviation (SD) for normally distributed continuous variables; categorical data are presented as a number and percentage. Differences between groups were compared using independent sample *t*-tests (means) and

chi-squared tests (categorical data). *P* values comparing three or more subgroups relate to data of one group vs other subgroups combined.

Informed consent was obtained from all participants. The survey was conducted in accordance with the Principles of the Declaration of Helsinki.

3 RESULTS

Between April and November 2015, 937 AF patients completed the survey from the United States (*n* = 322), Canada (*n* = 145), Germany (*n* = 160), France (*n* = 171), and Japan (*n* =139), with an overall mean (SD) age of 54.3 (16.6) years; 37.1% were female (Table 1). Of the 937 patients, 19.5%, 27.9%, and 29.8% demonstrated good, moderate, and low levels of stroke knowledge, respectively; 22.8% had no stroke knowledge. Stroke knowledge was independent of educational level, and significantly lower in those with AF and a recent stroke vs those with no recent stroke (32.5% of patients with a recent stroke had no stroke knowledge vs 20.3% of those without a recent stroke).

The most commonly known stroke symptoms were numbness/weakness/paralysis of the face, arm(s), leg(s) (known by 54.9% of patients), followed by confusion or trouble speaking or understanding speech (41.8%), dizziness (22.2%), trouble seeing/double vision (15.4%), and severe headache with no known cause (14.8%). The most frequently mentioned stroke risk factors were high blood pressure/hypertension (37.1%), smoking (26.8%), high cholesterol/hypercholesterolemia (19.7%), poor diet and/or lack of physical activity (17.4%), and AF (17.4%) (Supplemental Figure 1).

Familiarity with standardized information was stated to be good in 39% of patients overall, in 37% of patients with recently diagnosed AF without recent stroke, and in 53% of AF patients

with a recent stroke (Supplemental Table 5). Significantly more patients with the lowest levels of education (no school-leaving certificate) stated poor levels of familiarity with standardized information (37% vs 11–14% in other educational groups).

Overall, 39.4% of patients (47.5% with good stroke knowledge) perceived AF as extremely/very serious. Patients with good or moderate stroke knowledge were more often concerned about a stroke than those with no or low knowledge, who were more likely to never be concerned about a stroke (Table 1). Better stroke knowledge was associated with a preference for joint OAC treatment decision-making (Table 1) and with the use of more information sources about current OACs and higher utilization of health care professionals' advice (Supplemental Table 6).

Patients took a median of three different daily medications (interquartile range 2–6); 21.9% of patients took capsules/tablets once daily, 39.6% twice daily, and 38.5% ≥3 times daily.

3.1 Ranking Exercise

The attribute most often ranked as the most important was stroke prevention (47.4% of patients), followed by major bleeding risk (14.7%), other side effects (10.0%), dosing frequency (8.2%), antidote availability (7.8), dietary restrictions (7.0%), and administration with/without food (4.8%) (Figure 2). The proportions of patients who rated stroke prevention as the most important attribute increased as stroke knowledge improved (Figure 2).

3.2 Conjoint Analysis

All 937 patients completed a choice-based conjoint analysis; however, answers from 261 patients did not meet the quality assessments and were excluded, leaving 676 patients (232 in the United States, 104 in Canada, 94 in Japan, 123 in France, and 123 in Germany) (Supplemental Figure 2). Baseline characteristics are presented in Table 1.

Overall, patients valued stroke risk reduction as the most important OAC attribute, followed by major bleeding risk, frequency of administration, and administration with/without food, with utility values of 194.3, 115.9, 32.0, and 29.8, respectively. A 21% reduction in stroke risk vs standard therapy brings 77.5 points of utility, whereas a 20% reduction in major bleeding risk vs standard therapy results in 83.6 points of utility (Figure 3).

Stroke prevention was the most important attribute independent of stroke knowledge and was valued more highly in patients with better levels of stroke knowledge vs. those with lower levels of/no stroke knowledge (Figure 4). The relative level of importance placed on the four attributes was consistent across patient groups, regardless of their predefined AF subgroup, perceived seriousness of AF, concern about stroke and the frequency that they took oral medication (Supplemental Figures 3–6).

4. DISCUSSION

To our knowledge, this is the largest published study to assess OAC preferences among AF patients and is highly relevant to contemporary clinical practice, since patient values are increasingly featured in AF management guidelines. [1-3,20,21] OAC attributes relating to efficacy and safety were considered the most important in the ranking exercise and conjoint analysis, regardless of the AF subgroup, level of stroke knowledge, perception of seriousness of AF, concern about stroke, and the frequency of administration.

Unlike some previous surveys, [10,14] our study assessed stroke knowledge using open-ended questions, which may more accurately reflect a patient's level of understanding; asking patients to select from a list of potential answers may bias results. Patients with a recent stroke had significantly lower levels of stroke knowledge than those with no recent stroke, even though recent-stroke patients claimed to be highly familiar with the standardized information. Those with a recent stroke may have moderate disability or residual cognitive impairment, [22-24] which could limit their ability to enter free text or recall answers unaided in response to open-ended questions. Patients with recent stroke experience may also find it more challenging to confront risk factors associated with the condition, and devote less time to open-ended questions.

Better stroke knowledge was associated with using more information sources regarding current OACs, increased use of advice from health care professionals, and a preference for joint OAC treatment decision-making. Poor stroke knowledge was common and independent of educational level. Only 17.4% of patients named AF as a stroke risk factor, even though all respondents had AF. These findings highlight the need for improved healthcare professional-patient dialogue.

Pre-existing stroke knowledge did not affect the order in which OAC attributes were ranked in the ranking exercise or valued in the conjoint exercise, which were consistent. Information from a ranking exercise may be limited, as patients are likely to desire all of the benefits at no cost. Assessing patient-perceived values through a conjoint exercise forces patients into making a trade-off between positive and negative attributes, more accurately reflecting real life where one treatment is selected over others based on its individual profile. [25] Standardized information regarding AF, stroke and OACs was presented before the conjoint analysis, so that stroke knowledge was more consistent across the study population.

Our findings are consistent with those from other studies, in which efficacy and safety have been rated highly by patients. [6,26-28] Recent systematic reviews focusing on OAC preferences in AF patients showed that most patients valued stroke prevention over other attributes. [25,29] In a study by LaHaye et al, newly diagnosed AF patients were willing to suffer 4.4 major bleeds to prevent one stroke, demonstrating the importance placed on efficacy. However, 12% of patients in the study were unwilling to take antithrombotic therapy even if it was 100% effective. [28] Of note, our study only included patients taking OAC with an AF diagnosis dating back as far as 3 years; those unwilling to take antithrombotic treatment were excluded.

Although AF patients considered stroke risk reduction to be the most important OAC attribute in our study, an improvement of 21% over standard therapy appeared to be less compelling than a 20% reduction in major bleeding risk.

Our study is unusual in that we explored the potential impact of stroke knowledge and previous stroke on patient preferences regarding OAC attributes. The value placed on each attribute was consistent across all subgroups evaluated, including stroke knowledge and stroke history; interestingly, frequency of administration was of minor importance, regardless of the number of times per day that patients took oral medication.

The attributes evaluated in the conjoint analysis were chosen because each had a manageable number of permutations and could be used to differentiate the currently available NOACs. Dabigatran and apixaban are administered twice daily; edoxaban and rivaroxaban are dosed once daily and, unlike the other NOACs, rivaroxaban must be taken with food. Dabigatran is the only available NOAC for which a specific reversal agent (idarucizumab) is available. However, as the survey was conducted largely before its introduction, reversal agent availability was not included as an attribute.

Previous conjoint analyses or discrete choice experiments focusing on OACs generally included modest patient numbers and were not always limited to patients eligible for OAC. [27,30] In addition some have excluded efficacy and/or safety attributes, and consequently findings may. imply that patients place greater importance on convenience factors such as dosing frequency. [31,32] The results of our analysis suggest that stroke prevention and major bleeding risk are by far the most important factors that concern patients when selecting an OAC.

Study Limitations

This study has certain limitations. Online methodology may have introduced bias toward younger patients, males, and those with a higher educational level, however, preferences for OAC attributes were independent of age, sex and educational level (data not shown). In addition, the survey reflects the views of AF patients taking OACs, whereas in clinical practice a considerable proportion of patients are not treated with OACs despite a clear indication. [33,34]

In conclusion, the findings of our study suggest that efficacy and safety are considered to be the most important OAC attributes by the majority of AF patients. Dosing frequency was found to be of minor importance to most AF patients, irrespective of stroke knowledge, medication burden, perception of seriousness of AF, or concern about stroke. Understanding patients' needs and preferences with regards to OAC treatment will improve clinical outcomes, and as such we believe that our findings should be considered when discussing and selecting OACs with AF patients.

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Table/Figure legends

TABLE 1 Patient characteristics, perceptions and preferences

FIGURE 1 Example of one display of hypothetical product profiles presented to patients.

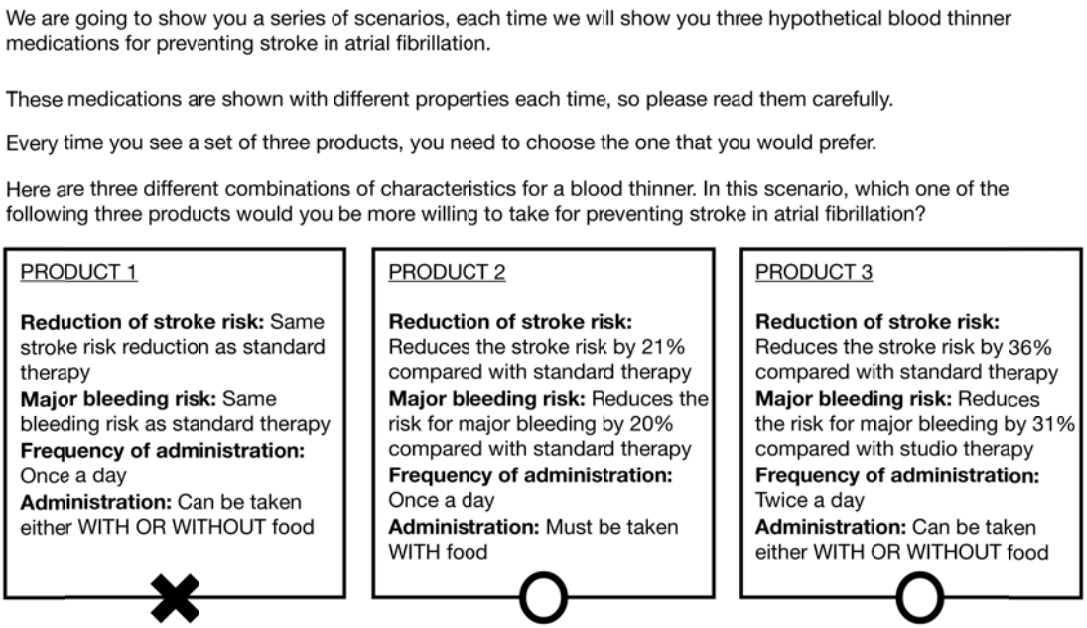

FIGURE 2 OAC attributes rated most important in ranking exercise.

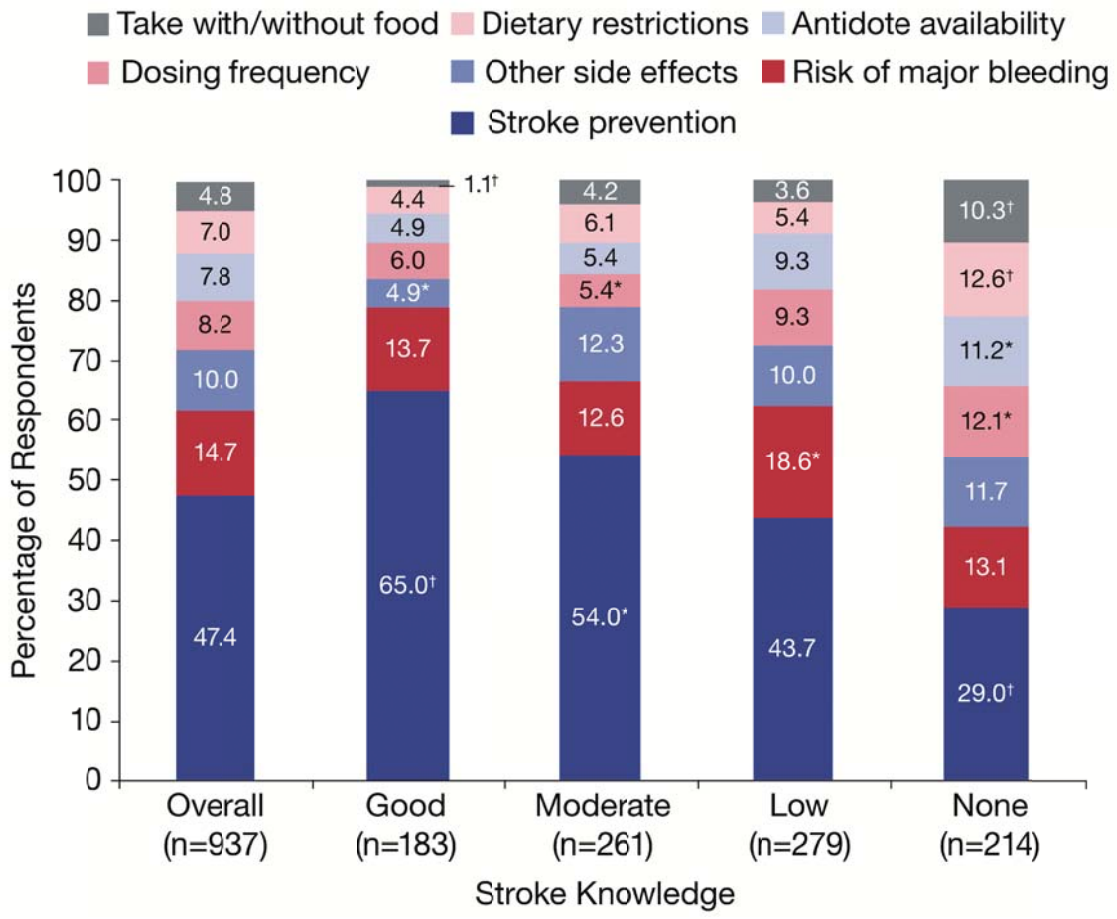

FIGURE 3 Relative gain in utility values determined from conjoint analysis.

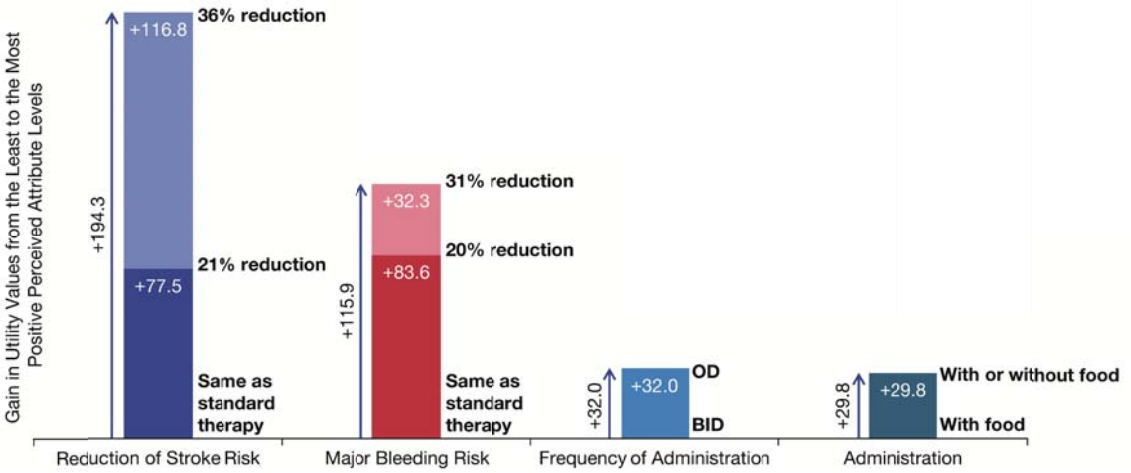

FIGURE 4 Relative gain in utility values according to stroke knowledge.

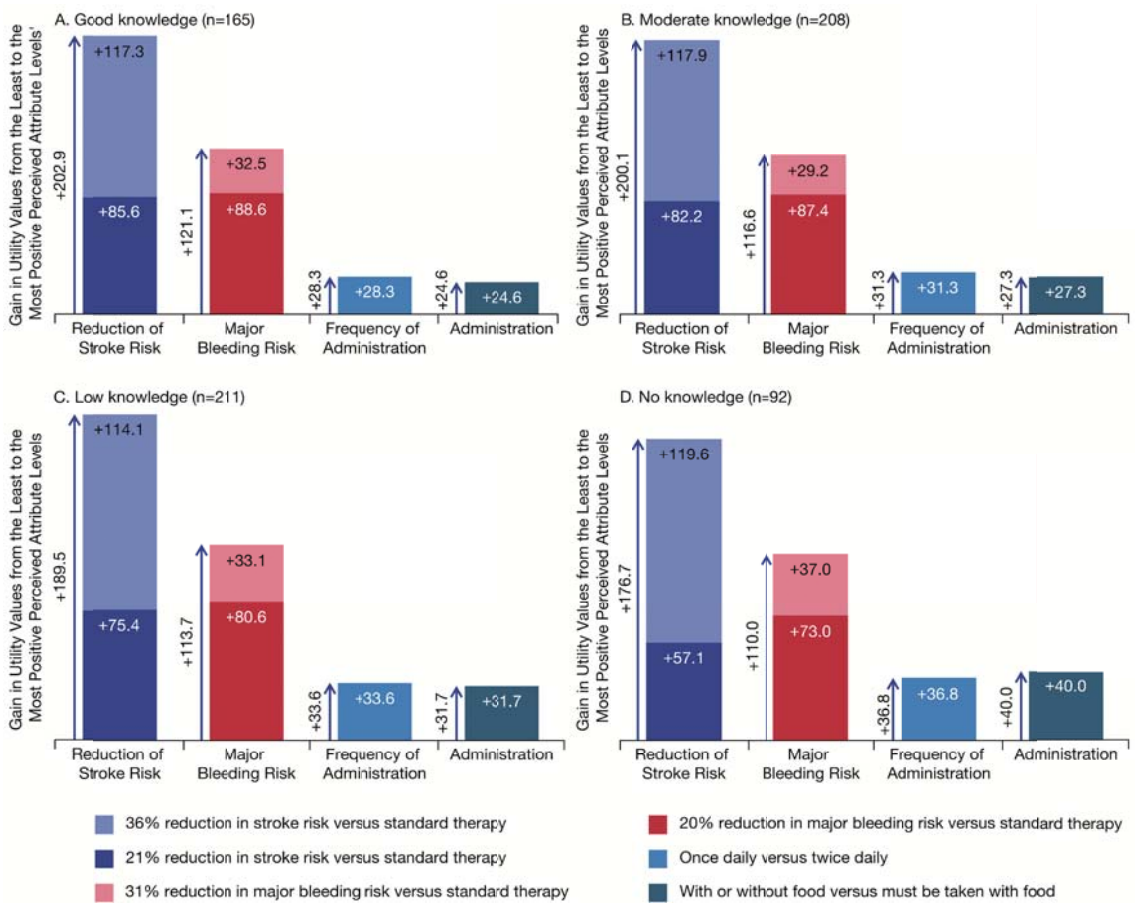

TABLE 1 Patient characteristics, perceptions and preferences

		Stroke knowledge				Conjoint analysis patients
	Overall	Good	Moderate	Low	None	
N (%)	937 (100)	183 (19.5)	261 (27.9)	279 (29.8)	214 (22.8)	676 (100)
Age, mean (SD) y	54.3 (16.6)	60.7 (12.4)[a]	57.2 (15.0)[a]	53.9 (17.0)	45.7 (17.4)[a]	57.6 (15.5)
≥65 y, n (%)	309 (33.0)	78 (42.6)[a]	104 (39.8)[a]	86 (30.8)	41 (19.2)[a]	268 (39.6)
Female, n (%)	348 (37.1)	77 (42.1)	104 (39.8)	96 (34.4)	71 (33.2)	256 (37.9)
CHA_2DS_2-VASc score, mean (SD)	2.6 (1.7)	2.8 (1.8)	2.7 (1.7)	2.6 (1.7)	2.5 (1.5)	2.6 (1.7)
Educational level, %[b]						
No school-leaving certificate	2.9	2.7	2.3	3.9	2.3	3.1
High school diploma	27.2	25.7	25.4	30.5	26.6	26.2
Community college	28.1	27.3	30.0	26.5	28.5	27.7

University/technical college	41.8	44.3	42.3	39.1	42.5	43.0
AF status, n (%)						
Newly diagnosed AF, no recent stroke	342 (36.5)	80 (43.7)	91 (34.9)[a]	99 (35.5)	72 (33.6)	265 (39.2)
Established AF, no recent stroke	401 (42.8)	84 (45.9)	117 (44.8)	121 (43.4)	79 (36.9)[c]	308 (45.6)
AF with recent stroke	194 (20.7)	19 (10.4)[a]	53 (20.3)	59 (21.1)	63 (29.4)	103 (15.2)
Perception of seriousness of AF, n (%)						
Extremely serious/very serious	369 (39.4)	87 (47.5)[c]	109 (41.8)	109 (39.1)	64 (29.9)[a]	268 (39.6)
Somewhat serious	390 (41.6)	76 (41.5)	110 (42.1)	113 (40.5)	91 (42.5)	282 (41.7)
Not at all/not serious	178 (19.0)	20 (10.9)[a]	42 (16.1)	57 (20.4)	59 (27.6)[a]	126 (18.6)
Concern about stroke, %						
Often/always	43.4	44.8	46.0	40.5	43.0	38.9

Occasionally	45.4	50.3	46.0	45.2	40.7	61.1[d]
Never/I don't know	11.2	4.9	8.0	14.3	16.4	
Patient preference for being involved in OAC treatment choice, %						
Doctor choice	44.7	26.8[a]	37.5[a]	50.5[c]	61.2[a]	
Patient–doctor choice	35.6	51.9[a]	42.5[a]	32.3	17.8[a]	
Patient choice	19.6	21.3	19.9	17.2	21.0	

Abbreviations: AF, atrial fibrillation, OAC, oral anticoagulant, SD, standard deviation.

[a]For stroke knowledge, $P < 0.001$ versus other groups pooled; [b]Data from 936 patients; [c]For stroke knowledge, $P < 0.05$ versus other groups pooled; [d]Never/occasionally.